We are committed to—

PROVIDING EFFECTIVE, PROACTIVE LEADERSHIP ON VACCINES AND IMMUNIZATION

The National Immunization Program provides effective, proactive leadership in the immunization arena by fostering sound vaccine recommendations and policies, conducting quality research, developing and distributing educational material, and enlisting and engaging the contributions of a wide range of professional and other organizations.

Assuring Vaccine Safety

As a leader in immunization safety research and surveillance, CDC plays a vital role in assuring vaccine safety. Sound immunization policies and recommendations affecting the health of our nation depend upon the continuous monitoring of vaccines and ongoing assessment of immunization benefits and risks. Through a multi-faceted approach, CDC's vaccine safety system identifies potential vaccine side effects, conducts epidemiological studies to determine whether a particular adverse event is associated with a specific vaccine, helps determine the appropriate public health response to vaccine safety concerns, evaluates public and health care provider perceptions of vaccination, and communicates the benefits and risks of vaccines to the public, media, and health communities.

Major Events of the Past Year *in Vaccine Safety*

Implementation of the Clinical Immunization Safety Assessment Network

Clinical Immunization Safety Assessment (CISA) centers represent a new initiative to improve the scientific understanding of vaccine safety at the individual "patient" level. This network of clinical academic centers, in partnership with CDC, will provide a source of clinical expertise in evaluating and treating adverse events following immunization. Clinically significant adverse reactions following vaccination are rarely seen in clinical trials, and health care providers see them too infrequently to be able to provide standardized treatment. At the CISA centers, people who believe they have suffered a severe adverse reaction following vaccination will be assessed, and information gathered from these assessments will be used to address knowledge gaps and to help prevent or reduce vaccine-related adverse events.

These centers include Johns Hopkins University partnering with specialists at the University of Maryland, Baltimore; Northern California Kaiser with collaborators at Stanford University in San Francisco, California and Vanderbilt University in Nashville, Tennessee; Boston University Medical Center in Boston, Massachusetts and Columbia Presbyterian Hospital in New York City, New York.

The primary goals of the CISA network include

- Developing protocols for the clinical evaluation and management of vaccine adverse events
- Improving the understanding of adverse events at the individual level (For example, it is hoped the CISA centers will help to identify genetic and other risk factors that may predispose individuals to adverse reactions to vaccines.)
- Serving as a public and health care provider regional referral center for clinical vaccine safety inquiries, such as taking referrals from pediatricians or family practitioners

Institutes of Medicine Immunization Safety Reviews

In the fall of 2000, CDC and the National Institutes of Health (NIH) requested that the National Academy of Sciences' Institute of Medicine (IOM) convene an Immunization Safety Review Committee. This independent expert committee is charged with examining three hypotheses about existing and emerging immunization safety concerns each year, through 2003. During 2002, the committee reviewed

- The possible association between Simian Virus 40 (SV40) contamination of polio vaccine and cancer
- The hypothesis that hepatitis B vaccine causes neurological disorders
- The hypothesis that vaccines could have a potential role in sudden unexpected death in infancy (A report has not been issued on this hypothesis at this time.)

Simian Virus 40 Contamination of Polio Vaccine and Cancer Safety Review

Background—Simian virus 40 (SV40) was discovered in 1960. It occurs naturally in some species of monkeys, though it does not typically cause symptoms or illness except in cases where the animal has chronic problems with its immune system. Soon after its discovery, SV40 was identified in polio vaccine. At the time, rhesus monkey kidney cells, which contain SV40 if the animal is infected, were used in preparing polio vaccine. Once the contamination was recognized, steps were taken to eliminate the virus from future vaccines. Interest in SV40 has increased in the last several years because the virus was found in certain forms of cancer in humans.

IOM Review and Conclusions—The IOM's Immunization Safety Review Committee found that the evidence is inadequate to accept or reject a causal relationship between SV40-containing polio vaccines and cancer. The committee also concluded that

1. Biological evidence is strong that SV40 is a "transforming" virus (that is, able to transform normal cells into malignant cells).
2. Evidence is of moderate strength that SV40 exposure could lead to cancer in humans under natural conditions.
3. Evidence is of moderate strength that SV40 exposure from polio vaccine is related to SV40 infection in humans.

Recommendations—In light of the biological evidence supporting the theory that SV40-contamination of polio vaccines could contribute to human cancers, the committee recommends continued public health attention in the form of policy analysis, communication, and targeted biological research. These recommendations include development of sensitive and specific blood tests for SV40 and a vaccine contamination and prevention plan. The committee did not recommend a review of the current use of polio vaccine on the basis of concerns about cancer risks because the vaccine used today is free of SV40. The polio vaccines that are being used today do not contain SV40. Also, the polio vaccines currently used in the U.S. (inactivated polio vaccine) is no longer prepared in primary rhesus monkey kidney cells.

Hepatitis B Vaccine and Neurological Disorders Safety Review

Background—In the United States, current recommendations call for all infants, adolescents, and high-risk adults to receive the hepatitis B vaccine for protection from serious liver disease, including cirrhosis and liver cancer. The Immunization Safety Review Committee reviewed the evidence regarding the hypothesis that the hepatitis B vaccine causes degenerative neurological disorders, such as multiple sclerosis and Guillain-Barré syndrome.

IOM Review and Conclusions—The IOM's Immunization Safety Review Committee reviewed findings from studies of vaccine-exposed populations and their comparison unvaccinated control groups of patients with these diseases and their comparison groups. Based on this evidence, the committee favored rejection of a causal relationship between the hepatitis B vaccine and multiple sclerosis. However, the evidence was inadequate to accept or reject a causal relationship between the hepatitis B vaccine and other known degenerative conditions.

Recommendations—The committee recommended further public health research and communication to increase understanding of hepatitis B vaccine recommendations in the United States. However, the committee did not recommend that national and federal vaccine advisory groups review the hepatitis B vaccine because of concerns about degenerative disorders.

continues

Significant Achievements *in Vaccine Safety*

Vaccine Safety Monitoring and Research Programs and Initiatives

The Vaccine Adverse Event Reporting System (VAERS) is a program for vaccine safety monitoring coordinated by the CDC and the Food and Drug Administration. The Vaccine Adverse Event Reporting System collects and analyzes reports of possible side effects and reactions that occur after the administration of U.S. licensed vaccines. Under the Vaccine Injury Compensation Act, health care providers and vaccine manufacturers are required to report certain adverse reactions following vaccination; however, anyone can report a suspected adverse event to VAERS. Vaccine recipients or their parents or guardians are encouraged to seek help from their health care professional in filling out the VAERS form.

Each year about 10,000 to 13,000 VAERS reports are filed directly by health care professionals, parents, patients, and through vaccine manufacturers. All reports are accepted and entered without determining whether the adverse event could have been caused by the vaccine in question. Approximately 89 percent of the reports describe mild and expected events such as fever, local reactions, episodes of crying or mild irritability, and other less serious experiences. Reports of more serious adverse events are investigated, and those investigations often find that many of the reported adverse events are not caused by vaccines.

Recent enhancements to the VAERS system include the availability of a free public-use dataset and the ability to report adverse events through the Internet. Both are accessible through the VAERS web site at ***www.vaers.org***

These improvements will make reporting easier and faster, as well as improve public access to VAERS information.

The Vaccine Safety Datalink (VSD) is a database containing comprehensive medical and immunization histories of over 7.5 million people. This project is a collaborative effort between CDC and several managed care organizations. The database makes it possible to conduct research studies that compare the prevalence of health problems between unvaccinated and vaccinated people. This improves the ability to determine whether adverse events following immunization are causal or coincidental. The VSD has recently grown from 4 to 8 managed care organizations, is more geographically diverse, incorporates multiple health systems models, and currently includes more than 2.5 percent of the U.S. population.

In 2002, CDC and its managed care partners established a new vaccine safety data-sharing process. This process allows external researchers to access data collected by the CDC's Vaccine Safety Datalink Project through the agency's Research Data Center in Hyattsville, Maryland. A process has been developed by CDC that permits researchers access to the VSD data while assuring protection of confidential medical information. Researchers submit their request to the VSD project outlining which area of vaccine safety they intend to investigate and which VSD files are needed. In accordance with federal regulations, each proposal must then be approved by the institutional review board at each managed care organization whose data will be used in the study. After receiving approval, researchers must follow standard, federally required guidelines to protect confidentiality and privacy of individuals and institutions.

The Brighton Collaboration is an international voluntary collaboration formed to develop globally accepted and implemented standardized case definitions for adverse events following immunization. These will be known as the Brighton Standardized Case Definitions. The project began in 2000 with the formation of a steering committee and the creation of the first six working groups. The working groups are comprised of international volunteers with expertise in vaccine safety and in work collaboration with regulatory, public health, scientific, professional, and vaccine manufacturing agencies. The guidelines for interpreting, recording, and presenting safety data developed by the collaboration will facilitate the sharing and comparison of vaccine data among vaccine safety professionals.

The Vaccine Identification Standards Initiative (VISI) is a joint, voluntary, cooperative effort between NIP and various partners in the vaccine and immunization system. The group's objective is to establish uniform guidelines and resources for vaccine packaging, labeling, and recording. These guidelines will enhance the safety of vaccination as well as the accuracy and convenience of transferring vaccine identifying information into medical records and immunization registries. They will also help monitor any adverse reactions following vaccination and assist in tracking vaccine lots for safety surveillance. For example, the VISI guidelines include standardized information on carton sidebars as well as barcoded peel-off stickers on vaccine vials and pre-filled syringes. The overall scope and content of the VISI application guidelines have been completed. In 2003 the guidelines will be compiled into a document for public comment and final publication.

Vaccine Safety Research Studies in 2002

The National Immunization Program conducts ongoing vaccine safety monitoring and research to determine if particular adverse events are associated with vaccines. Numerous studies were conducted and published in 2002.

Wheezing, lower respiratory disease, and vaccination of full-term infants

Pharmacoepidemiology and Drug Safety, 2002; 11(1): 21–30

Some previous studies have suggested that childhood vaccines may increase the risk of asthma. This matched, case-control study assessed the possible associations between vaccines and incidence of wheezing in full term infants born into the Kaiser Permanente Northwest health plan during 1991–1994. A total of 1366 case-control pairs were studied. No association was found between wheezing during infancy and receipt of childhood immunizations.

Childhood vaccinations and risk of asthma

Pediatric Infectious Disease Journal, 2002; 21(6): 498–504

A large cohort study involving 167,240 children was conducted to evaluate the suggested association between childhood immunizations and risk of asthma. The children involved in this study were enrolled in four large health maintenance organizations during 1991–1997. The study did not find an association between diphtheria, tetanus and whole cell pertussis, oral polio, or measles, mumps and rubella vaccines and the risk of asthma. A weak association was found between *Haemophilus influenzae* type b (Hib) and hepatitis B vaccines and asthma, which may have been caused by health care utilization or information bias.

Influenza vaccination is not associated with a reduction in the risk of recurrent coronary events

American Journal of Epidemiology, 2002; 156(7): 634–640

It has been suggested that acute respiratory infections, including influenza, may increase the risk of acute cardiac events. This study examined 1,378 Group Health Cooperative enrollees who experienced a first myocardial infarction in 1992–1996 to determine if receiving the influenza vaccine reduced the risk of recurrent coronary events. The results of this study suggest that the influenza vaccine does not protect older adults against recurrent coronary events.

Anthrax Vaccine Safety

In 1998, Secretary of Defense William S. Cohen initiated a program to vaccinate all U. S. active duty and reservist service personnel with anthrax vaccine (AVA). Concerns over this program, specifically related to the safety of AVA, led the U.S. Congress to appropriate funds for a collaborative effort by the CDC, NIH, and the Department of Defense (DoD) to study the safety and efficacy of AVA. The National Immunization Program is specifically responsible for studying anthrax vaccine safety as well as examining the knowledge, attitudes, and beliefs regarding anthrax vaccination. The NIP was involved in the following anthrax vaccine safety activities in 2002.

The Walter Reed National Vaccine Health Care Center

The Walter Reed National Vaccine Health Care Center opened in September 2001. This is the first vaccine health care center (VHC) in the country and the first in what is expected to be a network of centers coordinated by CDC and DoD. The centers will conduct follow-up and case management of certain military personnel who have experienced adverse reactions following anthrax vaccination. The knowledge gained from the VHCs will be used to improve the safety and quality of future vaccinations and to increase military personnel's confidence in the safety of DoD required vaccines. In addition, the VHCs are expected to help improve reporting of vaccine associated adverse events and facilitate further research on adverse events possibly related to vaccination.

Anthrax Vaccine Safety Research

In collaboration with CDC's National Center for Infectious Diseases (NCID), NIP has implemented a multicenter clinical trial to determine if the anthrax vaccine is safe and effective when administered through a different route and in fewer doses. Participant enrollment began in early 2002 and, as of December1, 2002, more than one third of the total enrollment goal (1,650 participants) had been met.

Bioterrorism Response

In collaboration with NCID, NIP implemented the Anthrax Vaccine and Antibiotic Availability Program for the administration of anthrax vaccine to civilians who were exposed to, or potentially exposed to, *B. anthracis* spores following the bioterrorist attacks in the District of Columbia, New Jersey, New York, Connecticut, and Florida. NIP has continued to monitor program participants for adverse events and submitted a 2002 annual report for the program to the Food and Drug Administration (FDA).

In June 2002, NIP collaborated with NCID to implement the Anthrax Vaccination Program (AVP), which offers pre-exposure anthrax vaccine to groups at risk for repeated exposures to *B anthracis* spores. Groups at risk for repeated exposure include laboratory personnel handling environmental specimens (especially powders) and performing confirmatory testing for *B. anthracis* in the U.S Laboratory Response Network for Bioterrorism Level B laboratories or above; workers who will be making repeated entries into known *B. anthracis* spore-contaminated areas after a terrorist attack; and workers in other settings in which repeated exposure to aerosolized *B. anthracis* spores might occur. As of December 1, 2002, approximately 480 people have received at least one dose of anthrax vaccine via the AVP. NIP has also designed and implemented the following three research studies in association with the AVP

1) Survey of Persons Eligible to Participate in the Anthrax Vaccination Program to determine how people make their decision to accept or decline the anthrax vaccine
2) Comparative Evaluation of the Effect of Anthrax Vaccine Absorbed on Health Related Quality of Life—Comparing Vaccinated to Unvaccinated Workers
3) Evaluation of the Effects of Hormonal Phase on the Occurrence of Local Adverse Events Following Immunization with Anthrax Vaccine in Women

Anthrax Vaccine Communication Activities

The National Immunization Program conducted the following activities to further enhance communication with the public and health care providers about anthrax vaccination.

- Development of a protocol to conduct a national survey of the knowledge, attitudes, and beliefs (KABs) among military personnel and military health care providers regarding the anthrax vaccine and a survey of military and civilian vaccine health care providers' KABs regarding reporting to VAERS
- Development of web based enhanced reporting of anthrax vaccine-associated adverse events to VAERS
- Initial development of standardized case definitions for anthrax vaccine associated adverse events (Brighton Collaboration)

Vaccine Risk Communication Activities

Research

The National Immunization Program's Vaccine Risk Communication and Research team regularly conducts research to better understand health professional and public vaccine safety KABs. Research activities conducted in 2002 include studies to examine parents' KABs regarding childhood immunizations, characteristics of children missing two or more routine vaccinations, and alternative health issues. The team also develops materials that effectively communicate information about vaccine risks and benefits.

Printed Materials

New materials, including brochures, fact sheets, question and answer documents, and resource kits on a variety of topics are regularly produced to keep health care providers, parents, and the public abreast of the most current information on vaccine benefits and risks. In 2002 a brochure was developed to help providers effectively communicate with parents who question or refuse immunizations for their children, in addition to a vaccine safety brochure for providers.

Website

The National Immunization Program frequently updates its website *(www.cdc.gov/nip)* to ensure that accurate and timely information can be easily found on vaccine benefits, risks, and safety.

National Immunization Information Hotline

Parents, patients, and health care professionals often call the National Immunization Information Hotline when they have questions or want the most current information on vaccine safety. The toll-free calls can be answered in both English and Spanish, and Tele-Typewriter and American Sign Language services are available to accommodate the hearing impaired. In 2002, the hotline staff responded to more than 111,000 calls about immunization issues.

Future and Continuing Activities
in Vaccine Safety

- Increase our knowledge of genetic risk factors for vaccine reactions.
- Utilize information in immunization registries to enhance vaccine safety efforts.
- Increase opportunities for research studies on vaccine risks by qualified external organizations and researchers.
- Improve vaccine benefit-risk communication, including parent and health care professional education, through expanded research and partnerships.

Success Story

VACCINE SAFETY

Studies Do Not Find a Link Between Vaccines and Childhood Asthma

Studies conducted throughout the world have helped dispel the theory that childhood vaccines, especially those containing the pertussis vaccine might increase a child's risk of developing asthma. For example, a large clinical study in Sweden and a longitudinal study in the United Kingdom discovered that children who received the pertussis vaccine did not have an increased risk of asthma or wheezing. This was supported by two additional studies from the Vaccine Safety Datalink.

Research studies have also dispelled the theory that the influenza vaccine can cause children with asthma to suffer an attack. In fact, one study suggested that asthmatic children who received the influenza vaccine may have a decreased risk of asthma attacks during the influenza season. Overall, the proven benefits of vaccination outweigh any theoretical risk of asthma attacks.

POLICIES AND RECOMMENDATIONS

2002 RECOMMENDATIONS FROM THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

(A panel of multi-disciplinary experts who provide immunization advice and guidance to the federal government).

Prevention and Control of Influenza

MMWR Weekly Report 51(RR–03); 1–31, 2002

The Advisory Committee on Immunization Practices (ACIP) updated the recommendations for the use of the influenza vaccine. The 2002 recommendations cover the following major areas:

Timing—While the optimal time to receive the influenza vaccine is October and November, the ACIP recommends that vaccination efforts in October focus on those at greatest risk of influenza-related complications and their household contacts and on health care workers. Vaccination of other groups should begin in November. Vaccination for all groups should continue into December and later, for as long as the vaccine is available.

Pediatrics—Children younger than 6 months of age cannot receive the influenza vaccine; therefore, household contacts of these children are recommended to get the first vaccine available to prevent transmitting influenza to these children. In addition, providers and parents should be reminded that children between 6 and 23 months of age are at increased risk of hospitalization if they are infected with the influenza virus. While a formal recommendation has not been made at this time to vaccinate all children older than 6 months of age against influenza, providers and parents are strongly encouraged to give these children that protection whenever feasible.

Thimerosal—A limited amount of influenza vaccine with reduced thimerosal content was available for the 2002–2003 influenza season.

Use of Anthrax Vaccine in Response to Terrorism: Supplemental Recommendations of the ACIP

MMWR Weekly Report 51 (RR–45); 1024–1026, 2002

The supplemental recommendations for the use of anthrax covered three major areas:

Use of anthrax vaccine for pre-exposure vaccination—
The following groups who are at risk for repeated exposures to *B. anthracis* spores are recommended to be given priority for pre-exposure anthrax vaccination: laboratory personnel handling environmental specimens (especially powders) and performing confirmatory testing for *B. anthracis* in the U.S Laboratory Response Network for Bioterrorism Level B laboratories or above; workers who will be making repeated entries into known *B. anthracis* spore-contaminated areas after a terrorist attack; and workers in other settings in which repeated exposure to aerosolized *B. anthracis* spores might occur.

Prevention of anthrax by postexposure prophylaxis (PEP)—
The ACIP endorses CDC making anthrax vaccine available in a 3-dose regimen in combination with antimicrobial PEP. This should be administered under an Investigational New Drug application with the Food and Drug Administration to unvaccinated people who are at risk for inhalational anthrax. However, anthrax vaccine is not licensed for post-exposure use in preventing anthrax.

Recommendations for additional research—
Additional research is recommended on the safety and efficacy of anthrax vaccine for children and for pregnant women. The ACIP also recommends research on developing an improved vaccine for preventing anthrax as well as new therapeutic strategies.

General Recommendations on Immunization

MMWR Weekly Report 51(RR–02); 1–36, 2002

The principal changes include expansion of the discussion of vaccination spacing and timing, recommendations for vaccinations administered by an incorrect route, information regarding needle-free injection technology, vaccination of children adopted from countries outside the United States, timing of live-virus vaccination and tuberculosis screening, expansion of the discussion and tables of contraindications and precautions regarding vaccinations, and addition of a directory of immunization resources.

Institute Of Medicine Reports

Calling the Shots: Immunization Finance Policies and Practices

In 2000, the Institute of Medicine (IOM) released its report, *Calling the Shots: Immunization Finance Policies and Practices*, which examined the roles and responsibilities of state and federal governments in supporting immunization programs and services. The IOM formed the Committee on Immunization Finance Policies and Practices to look particularly at one of the programs administered by the CDC—the Section 317 program that makes annual awards to states to help them purchase vaccines and support immunization programs. The IOM report recommended additional federal and state funding to purchase vaccines for the nation's poorest individuals and greater financial and administrative support for state and local immunization programs. The IOM also recommended that federal and state agencies develop a set of consistent immunization monitoring measures. Regional meetings were held in Chicago, Austin (Texas), and Los Angeles, and a national meeting was held in Washington, D.C. to promote the study's conclusions and recommendations. Summaries of the Chicago and Austin meetings, which emphasized regional and local issues, have already been published. The other meeting reports will be published in early 2003.

Purchasing recommended vaccines: Financing options for public and private sector in the United States

In 2002, the IOM started a follow-up study designed to help identify the most effective ways to finance the purchase and delivery of vaccines. The new study, *Purchasing recommended vaccines: Financing options for the public and private sectors in the United States* will address five questions:

1. What are the roles and responsibilities of public and private agencies and health care providers in financing the purchase and administrative costs of vaccines to achieve national immunization objectives for all children, adolescents, and adults in the U.S.?
2. In working towards an appropriate balance of roles and responsibilities, what finance strategies best achieve national goals and best fit the service delivery mechanisms for various vaccines and population groups?
3. What are the current levels of need for recommended vaccines in the child, adolescent, and adult populations for those persons who do not have health plan benefits that include immunizations or who have large co-payments or deductibles?
4. What methods could reduce the time lag and disparities that occur between new vaccine recommendations and the availability of public and private financing to implement the recommendations?
5. Will vaccine products under consideration for licensing have a significant effect on future vaccine purchase strategies in public and private health plans?

The IOM Committee on the Evaluation of Vaccine Purchase Financing in the United States met four times in 2002 and hopes to release their findings in a report mid-2003.

IOM Report on CDC's Anthrax Vaccine Research Plan

The Institute of Medicine's Committee to review the CDC's anthrax vaccine safety and efficacy research plan issued its final report on October 15, 2002. The committee found the CDC's response to the Congressional mandate to be generally complete and appropriate.

In collaboration with the DoD's Army Medical Surveillance Activity and the FDA, CDC is establishing a joint research project to conduct hypothesis generation and hypothesis testing for rare adverse events potentially associated with the anthrax vaccine using the Defense Medical Surveillance System's database. A research advisory board will also be created to assist in prioritizing research questions to be addressed through project protocols.

Government Performance and Results Act

The Government Performance and Results Act (GPRA) was enacted in 1993 to improve accountability in all federal agencies through the development of measurable objectives.

In 1998, CMS developed their childhood GPRA objective to increase the number of fully immunized two-year-old children enrolled in Medicaid and requested that the CDC partner with them on this important objective. The CMS immunization objective is implemented at the state level, and currently all states and the District of Columbia are participating. At the state level, both the state Medicaid agency and state immunization program collaborate to develop and obtain a baseline measure of the immunization coverage levels of the 2-year-olds enrolled in Medicaid. They also set improvement goals, implement strategies to achieve the goal, and continue to measure the coverage level. Technical assistance is provided by the Centers for Medicare and Medicaid and the CDC to the states on many different aspects of the GPRA objective.